

# Caries experience by socio-behavioral characteristics in HIV-1 infected and uninfected Ugandan mothers - a multilevel analysis

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## Research article

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# Abstract

**Background:** Few studies consider the oral health status of adults with HIV in comparison with negative controls. This study aims to assess caries experience in Ugandan mothers according to HIV status, socio-behavioral-characteristics and gingival bleeding status and to examine whether HIV status modifies the association of socio-behavioral characteristics with caries experience. Secondly, using multilevel analysis this study also assessed to what extent site specific caries experience vary between and within individuals.

**Methods:** This study uses data from the Ugandan site of the ANRS 121741 PROMISE- PEP trial (ClinicalTrials.gov, number NCT00640263) conducted in 2009-2013 that recruited mothers with HIV-1. In 2017 a comparison group of 181 HIV-1 negative controls was recruited. Caries experience was recorded using the World Health Organization's Decayed, Missed and Filled teeth/surfaces (DMFT/DMFS) indices. Mixed effects logistic regression with the melogit program within Stata was conducted with DMFT/DMFS as the outcome and HIV-1 infection status as well as socio-behavioral characteristics as exposures.

**Results:** Caries experience differed statistically significantly between HIV infected and non-infected mothers with 81% and 71% having DMFT>0, respectively. The corresponding mean and standard deviation were 4.6 (5.3) and 2.8 (3.2) respectively. Mixed effect logistic regression revealed significant positive associations between site specific caries and women's age (OR=1.8, 95% CI: 1.1–2.8), and presence of gingival bleeding (OR =2.0, 95% CI: 2.0 1.2–3.2). Compared to premolar teeth, caries experience was more likely to occur in maxillary molars and mandibular molars and less likely to occur in incisors. The intra class correlation (ICC) for the correlation of individuals was 0.54 (95% CI: 0.48–0.59). No two-way interactions terms between HIV-1 status and socio-demographic, behavioral and clinical covariates were observed.

**Conclusion:** The prevalence of dental caries is higher in Ugandan mothers with HIV-1 than in uninfected Ugandan mothers and varies with mothers', age, education and clinically recoded gingival inflammation. Socio-demographic differences in dental caries did not vary by HIV-1 status. We found that a multilevel random intercept model is appropriate and efficient for analyses of site specific dental caries data in the context of HIV-1 infected and uninfected Ugandan mothers

## Background

Following widespread implementation of highly active anti-retroviral drugs (HAART), studies have shown an increase in life expectancy as well as in the prevalence of HIV-1 infected people worldwide [1]. Sub Saharan African countries are currently contributing 65% to the global total of 33 million people living with HIV [2]. Although people with HIV-1 are particularly vulnerable to oral diseases, studies examining their dental caries experience have so far been rare [3]. Some studies have reported increased dental caries prevalence in children with perinatally acquired HIV-1 infection [4–6]. It is unclear however, whether findings from those studies generalize to adult populations living with HIV /AIDS.

Evidence suggests that HIV-1 infection under HAART influences the oral microbiome, thus emphasizing the vulnerability of individuals with HIV-1 to oral microbial diseases [7]. Studies have reported on strong associations between HIV-1 infection and oral mucosal lesions and periodontal disease [8–11]. Moreover, the prevalence of oral lesions seems to increase with increasing level of immune suppression [12, 13]. Adults with HIV-1 not on HAART show a greater risk of presenting with oral lesions and periodontal pockets than adults with HIV-1 receiving HAART. There are indications however, that individuals with HIV-1 on long-term HAART medication have a greater risk of oral lesions than their counterparts on short-term medication [14].

Considering the association between HIV-1 infection and dental caries, data have been inconsistent. No difference in dental caries was observed between uninfected and perinatally exposed HIV uninfected children in Uganda [15]. In contrast, a Nigerian study comparing three groups of preschool children, reported higher caries prevalence in HIV infected than in HIV uninfected children, whereas no difference was found between HIV uninfected and HIV exposed uninfected children [6]. A systematic review considering caries in the primary and permanent dentition of children with HIV reported increased risk of caries in the primary but not in the permanent dentition [16]. Moscicki et al [17] reported on higher caries prevalence in youth with HIV compared with their exposed uninfected counterparts but no difference regarding periodontal disease. Women's Interagency HIV Study (WIHS), including the largest cohort of HIV infected women in the United States, revealed significantly higher caries scores (number of decayed, missed filled teeth, DMFT) in women with HIV compared to HIV negative women [18]. Moreover, reports reveal an increase in caries prevalence following HAART medication among people with HIV [19, 20] and suggest that the prevalence of dental caries varies according to the type and length of HAART medication taken [14]. A study in Uganda reported a caries prevalence of above 80% in HIV positive adults, whereas the corresponding parameters in the general adult population were estimated to 67%. This study also indicated that longer duration of HAART medication associated with increased risk of dental caries [20].

Factors, such as xerostomia, microbial colonization, poor oral hygiene, periodontal disease and carbohydrate diet increase susceptibility to dental caries in HIV infected adults [20]. Kumar et al [11] and Soares et al [21] reported on higher caries experience and higher prevalence of periodontal disease in HIV positive patients of low compared to high socio-economic status. A question arises as to whether oral diseases are more frequent in the lower compared to the higher socio-economic status groups of HIV infected people and whether social inequality in oral health status vary between HIV infected and uninfected individuals.

There is a paucity of studies considering the prevalence and socio-behavioral covariates of dental caries among adults with HIV-1 in Sub Saharan Africa. Previous studies have considered individuals attending HIV care clinics and many have omitted an adequate comparison groups of uninfected individuals. Moreover, studies examining dental caries generate multiple outcome data. An important caveat is avoidance of utilizing multilevel modeling for hierarchical clustered data. Ignoring that tooth surfaces are clustered within teeth and that teeth are clustered within individuals by using classic statistical methods might provide biased regression estimates and underestimated standard errors.

## Purpose

This study aims to assess caries experience in Ugandan mothers according to HIV-1 status, socio-behavioral characteristics and gingival bleeding status and examine whether HIV status modify the association of socio-behavioral covariates with caries experience. Secondly, using multilevel analysis, this study also assessed to what extent site specific caries experience vary between and within individuals.

## Methods

This cross-sectional study uses data from the follow-up of women with HIV-1 involved in the efficacy trial of clinical HIV-1 peri-exposure prophylaxis with ritonavir boosted lopinavir- (LPV/r), the ANRS12174 PROMISE- PEP trial (ClinicalTrials.gov, number NCT00640263). The ANRS12174 PROMISE- PEP trial is described in detail in previous papers [22]. The trial conducted between 2009 and 2013, was a multi-center randomized trial including pregnant women with HIV-1, recruited at gestational age of 28–40 weeks at antenatal clinics in four African sites; Ouagadougou, Burkina Faso; East London, South Africa; Mbale, Eastern Uganda; and Lusaka, Zambia. HIV-1 infected pregnant women were referred for further assessment of inclusion criteria and again with their HIV uninfected children for enrolment at day 7 postpartum. Infants were eligible for inclusion if they were: a singleton; breastfed at day seven by their mothers; had a negative HIV-1 DNA PCR blood test and had received any Prevention of-Mother-to-Child-Transmission, PMTCT. Inclusion criteria for mother was age 18 years or older, intention to continue breastfeeding, being HIV-1 infected, and not being eligible for ART (either clinically or because CD4 count > 350 cells/ $\mu$ L at that time). All eligible mothers and infants followed the routine PMTCT with antepartum zidovudine (ZDV), intrapartum nevirapine (NVP), zidovudine-lamivudine (ZDV/3TC) for mothers and NVP for infants 7 days postpartum.

In Uganda, 278, seven-day old uninfected children born to HIV-1 infected women were randomized to receive infant prophylaxis (either 3TC or LPV/r daily) throughout the breastfeeding period from day 7 to 50 weeks. The primary outcome was mother to child HIV-1 transmission, diagnosed at day 7 and 6, 14, 26, 38 and 50 weeks with HIV-1 DNA PCR between 7 days and 50 weeks post-delivery. Findings from the PROMISE- PEP trial showed that infection rates, and clinical and biological severe adverse events did not differ between the two drug regimens suggesting that infant HIV-1 prophylaxis with either drug was not superior as both led to very low rates of HIV-1 postnatal transmission during 50 weeks of breastfeeding [22].

In 2017, 244 out of 278 mothers with HIV-1 infection and their uninfected children were eligible for re-enrollment in the follow-up study: the PROMISE-PEP Mechanism Safety study (PROMISE-PEP M&S ANRS12341). Of the 166 HIV exposed uninfected children (HEU) re-enrolled, 2 were excluded because they had contracted HIV during the follow up period. Thus, 68% of the eligible cohort of HEU children (164/244) and their HIV-1 infected mothers were followed up with 32% (n = 112) missed due to attrition. A comparison group of 199 HIV unexposed uninfected (HUU) children matched on age and sex, as well as

their HIV uninfected mothers were recruited from communities located in Mbale, Eastern Uganda, which was the site for the ANRS12174 PROMISE- PEP trial. Of the 199 HUU control children, 19 were excluded due to a positive HIV-1 test result, leaving 181 HUU children and their uninfected mothers enrolled. The present cross-sectional study is based on information from interviews and clinical oral examinations of 164 HIV-1 infected- and 181 HIV-1 uninfected mothers participating in the follow-up study, the PROMISE-PEP Mechanism Safety study (PROMISE-PEP M&S ANRS12341) in 2017.

## **Interviews with HIV-1 infected mothers and HIV – 1 negative controls**

Trained interviewers performed face-to-face interviews with mothers using semi-structured interviews in one of the local Ugandan languages, Lumasaba. The interview was constructed in English and translated into Lumasaba for use in the field. The schedule had been reviewed previously by project staff for semantic, experiential and conceptual equivalence of the source version. Sensitivity to culture and selection of appropriate words were considered [22, 23]. Mothers responded to questions about themselves and their children. Information was documented on case record forms (CRFs) and electronically with Capture software System (Clinsight) and Epidata program [www.epidata.dk](http://www.epidata.dk) for the clinical oral examinations.

Socio-demographic characteristics of caretakers were assessed in terms of level of education, type of income and marital status. Level of education was categorized into 'did not finish primary school (1), end of primary school (2) higher education' (3). Marital status was categorized: 'divorced (1), cohabiting/married (2), single (3), widowed' (4) and recoded into single/divorced/widow (0) and married/cohabiting (1). Mother's behavioral characteristics were assessed in terms of tooth brushing frequency and frequency intake of sugared snacks. Type of income was categorized into (1) no regular income (2) regular income.

## **Clinical oral examination**

Two experienced and calibrated dental surgeons (NB and MM) performed the oral assessments among the study participants and duplicate full-mouth oral clinical examination among HIV-1 positive and HIV negative mothers not included in the main study. Dental caries was assessed on surface and tooth level (5 surfaces per tooth) in terms of decayed (D), missing (M), and filled (F) surface/teeth (DMFS/DMFT) in accordance with the World Health Organization (WHO) guidelines for field conditions [24]. Each surface was recoded 0 for sound and 1 for caries experience and documented as decayed if it was visually cavitated with the aid of a dental mirror and periodontal probe. A surface was recorded filled when treated and a tooth was recorded missing when extracted due to caries, as confirmed by the participant. To assess gingival bleeding of the individual, the modified community periodontal index (CPI) was used. Each tooth was scored according to the presence or absence of gingival bleeding, using a periodontal probe across the gingival margins of the teeth. An individual score of presence of gingival bleeding was given if a tooth had bleeding on probing.

# Maternal HIV-1 status of HIV-1 uninfected controls

Mothers in the comparison group were tested for their HIV-1 status using serial and parallel HIV rapid testing with Determine, Stat-Pak and Uni-Gold, three test algorithms as recommended by the Ugandan Ministry of Health [25].

## Statistical analysis

STATA SE 16 (College Station, Texas 77845 USA) was used for data analysis. Cross-tabulation and Chi-square tests for categorical variables were used to assess the crude associations of covariates and outcome variables according to HIV-1 status. Site specific dental caries data has a clustered 3-level hierarchical structure with surfaces (level 1) clustered within tooth (level 2) and teeth clustered within individuals (level 3). Using site specific measures of caries as independent observations and ignoring that observations are clustered and correlated within individual will lead to an underestimation of the standard errors, too narrow confidence intervals and higher type 1 error rates. In this study we first applied ordinary logistic regression on the individual level with aggregated measures of Decayed Missed and Filled Teeth (DMFT) as dichotomized outcome variable ( $DMFT > 0$ ). Socio-behavioral and clinical covariates statistically significantly associated both with HIV-1 status and DMFT were included in the ordinary logistic, and potential confounding variables. Secondly, we applied caries on all observed sites within individual. This was done using a random intercept model (RIM) (random intercepts for teeth and individuals) using mixed effect logistic regression with the melogit package within the Stata program (version SE 16) fitted for caries experience. Due to high correlation of caries on surface level within tooth, a three-level model including random intercepts for both individuals and teeth could not be fitted. Thus, we fitted a two-level model with sites within individuals. Relationships between outcome and covariates were assumed with all the cluster regression lines having a fixed slope and different intercepts. The effect of dependency of caries on sites within individual was assessed by calculating intra class correlation coefficients (ICC). The ICC expresses variations between individuals as a proportion of the total variance. ICC varies from 0, which implies that caries is independent within individuals to 1 indicating no variation of caries within individual. We applied a likelihood-ratio test to test if ICC equals 0. A statistical significance implies that the multilevel model is preferable. P-values less than 0.05 were considered statistically significant.

## Results

Cohen's Kappa values for intra- and inter-rater reliability were 0.7 (95% CI: 0.5–0.9) and 0.6 (95% CI: 0.4–0.8), respectively.

Table 1 provides descriptive analyses of independent and dependent variables at the individual level. A total of 164 HIV infected and 181 HIV uninfected mothers were interviewed and examined for dental caries and gingival bleeding. A total of 162 (50%) was younger than 33 years. Prevalence of individuals with decayed surfaces (i.e. proportion of participants with  $DMFS > 0$ ) was 74.%. Corresponding prevalence figure for decayed teeth (i.e. proportion of individuals with  $DMFT > 0$ ) was 61.%.

Table 1  
Socio-demographic- clinical and behavioral characteristics of mothers by HIV-1 status at follow-up in the Ugandan part of the PROMISE-PEP-M&S study.

	HIV- infected (n = 164)	HIV- un-infected (n = 181)	Total Individual (n = 345)
T	% (n)	% (n)	% (n)
<b>Mother /caretaker characteristics</b>			
<i>Age</i>			
18-32yr	40 (58)	58 (104)	50 (162)
33+	60 (90) **	42 (76)	50 (166)
<i>Toothbrush</i>			
Once a day or less	59 (97)	44 (78)	51 (175)
More than once a day	40 (66)	56 (99) **	48 (165)
<i>Sugared snacks</i>			
At most occasionally	92 (151)	88 (159)	90 (310)
At last once a day	8 (13)	12 (21)	10 (34)
<i>Marital status</i>			
Single/divorced, widow	26 (43)	18 (33)	22 (76)
Married/cohabiting	74 (121)	82 (147)	78 (268)
<i>Type of income</i>			
No regular	60 (98)	72 (130)	66 (228)
Regular	49 (65)	28 (51) *	34 (116)
<i>Educational level</i>			
Primary school	38 (54)	40 (65)	38 (119)
End of primary school	20 (28)	22 (37)	21 (65)
Middle school/high school/college	42 (59)	38 (63)	40 (122)
<i>DMFT</i>			
DMFT = 0	19 (31)	29 (52)	24 (83)

\* p < 0.05;  $\chi^2$ test, \*\* p < 0.001;  $\chi^2$ test

Numbers do not add to 345 in the various cells due to missing responses

	HIV- infected (n = 164)	HIV- un-infected (n = 181)	Total Individual (n = 345)
DMFT > 0	81 (133)	71 (129) *	3 (4.3)
DMFT ≥ 1	5 (5.3)	3 (3.2)	76 (264)
DT > 0	76.2 (125)	46 (84)	61 (209)
<i>DMFS</i>			
DMFS = 0	22 (37)	54 (29.8)	26 (91)
DMFS > 0	77 (127)	70 (127)	74 (254)
DS > 0	93 (51)	120 (73.2)	62 (213)
<i>Mothers health</i>			
Bad/fair	35(57)	18 (33)	26 (90)
Good/very good	82 (147)	65 (107) **	74 (254)
<i>Presence of gingivitis</i>			
No	35 (58)	56 (102)	46 (160)
Yes	64 (105)	44 (79) **	54 (185)
* p < 0.05; $\chi^2$ test, **p < 0.001; $\chi^2$ test			
Numbers do not add to 345 in the various cells due to missing responses			

The distribution of participants' socio-demographic-, behavioral and clinical characteristics according to mothers' HIV-1 status are presented in Table 1. Age, marital status, type of income, mothers' perceived health, gingival bleeding, and caries experience varied statistically significantly (all  $p < 0.05$ ) according to HIV-1 status. Mothers with HIV-1 were more frequently older than 33 years of age, were less likely to brush teeth more than once a day, less likely to be married and more likely to have regular income compared to HIV negative mothers. Mothers with HIV-1 were more likely to express bad perceptions of health and to present with gingival bleeding.

Table 2 depict percentage distribution, odds ratios (OR) with 95% confidence intervals for dental caries experience (DMFT > 0/DMFT ≥ 1) by HIV-1 status and socio-behavioral and clinical covariates. Significant crude association occurred between caries experience and HIV-1 status, educational level, perceived health and presence of gingival bleeding. Caries experience differed statistically significantly between HIV-1 infected and non-infected mothers with 81% and 71% having DMFT > 0, respectively. Moreover, 82% versus 69% of mothers with and without presence of gingival bleeding presented with DMFT > 0. Ordinary adjusted logistic regression analysis revealed that HIV-1 infected mothers were more likely than their HIV-1 negative counterparts to experience DMFT > 0 (OR = 1.8, 95% CI 1.0–3.4). Mothers

with higher education (high school and college) were more likely to experience caries compared to their lower educated counterparts (OR = 1.9, 95% CI: 1.0–3.6). Moreover, mothers presenting with gingival bleeding were more likely to present with caries experience (OR = 2.1, 95% CI: 1.1–3.8). Two-way interactions terms between HIV-1 status and each of the socio-demographic, behavioral and clinical covariates were added to the regression model after adjustment for the main effect of the variables included in the multiplicative constructs. No significant interactions were observed.

Table 2

Mothers' dental caries experience according to individual related factors in terms of HIV status, socio-demographic – and behavioral/clinical characteristics. Adjusted ordinary logistic regression (n = 345)

Mothers characteristics	Cross tabulation	Adjusted Ordinary logistic regression DMFT > 0
HIV-1 Status	% (n)	OR (95% CI) <sup>e</sup>
HIV-1 uninfected	71 (129)	1
HIV-1 infected	81 (133) *	1.8 (1.0–3.4)
<i>Age</i>		
18–32	72 (117)	1
33+	79 (132)	1.5 (0.8–2.7)
<i>Marital status</i>		
Single/divorced, widow	79 (60)	1
Married/cohabiting	75 (202)	1.0 (0.6–2.1)
<i>Type of income</i>		
No regular	67 (175)	1
Regular	33 (86)	0.9 (0.5–1.8)
<i>Educational level</i>		
Primary school	74 (88)	1
End of primary school	71 (46)	0.8 (0.4–1.8)
Middle school/high school/college	82 (100)	1.9 (1.0–3.6)
<i>Gingivitis</i>		
Not present	69 (110)	1
Present	82 (152) **	2.1 (1.1–3.8)
* p < 0.05; $\chi^2$ test, ** p < 0.001; $\chi^2$ test, <sup>e</sup> odds ratio 95% confidence interval		
Numbers do not add to 345 in the various cells due to missing responses		

Table 3 depicts the fixed effects on site specific caries of mothers' HIV-1 status, socio-demographic factors, gingival bleeding, tooth groups and tooth surfaces. In the multilevel logistic regression analysis, a total of 46095 surfaces and a mean number of 158 (range 140–160) surfaces per individual of were analyzed.

Table 3

Mothers' dental caries experience according to HIV-1 status, age, marital status, education, gingivitis, tooth groups and surfaces. Multilevel analysis (melogit) allowing for clustering at individual level (n = 46095).

<b>Mothers characteristics</b>	<b>Adjusted melogit DMFS &gt; 0</b>
HIV-1 Status	OR (95% CI) <sup>e</sup>
HIV-1 uninfected	1
HIV-1 infected	1.4 (0.8 – 2.2)
Age	
18–32	1
33+	1.8 (1.1–2.8)
Marital status	
Single/divorced, widow	1
Married/cohabiting	1.1 (0.6–2.0)
Type of income	
No regular	1
Regular	0.9 (0.5–1.6)
Educational level	
Primary school	1
End of primary school	0.8 (0.4–1.4)
Middle school/high school/college	1.2 (0.7–2.1)
Gingivitis	
Not present	1
Present	2.0 (1.2–3.2)
Tooth group	
Premolars	1
Molars- maxilla	7.4 (6.6–8.3)
Molars mandibular	17.0 (15.2–18.2)

Values are person specific estimates adjusted for tooth group, surfaces and individual level covariates calculated using a melogit multilevel regression model with a random intercept

<sup>e</sup>Odds ratio (95% confidence interval)

Mothers characteristics	Adjusted melogit DMFS > 0
Incisor	0.5 (0.4–0.7)
Surfaces	
Buccal	1
Distal	1.1 (0.9–1.2)
Mesial	1.1 (0.9–1.2)
Occlusal	0.9 (0.8–1.1)
Palatal/lingual	2.7 (2.4–3.0)
ICC within subject (adjusted for covariates)	0.54 (0.48–0.59)
Random effect	3.8 (3.0–4.8)
Model fit	4297.60; P < 0.0000
AIC	18498.95
Values are person specific estimates adjusted for tooth group, surfaces and individual level covariates calculated using a melogit multilevel regression model with a random intercept	
°Odds ratio (95% confidence interval)	

The multilevel model revealed significant positive associations between caries and women older than 33 years of age (OR = 8.1, 95% CI: 1.1–2.8), and between caries and presence of gingival bleeding (OR = 2.0, 95% CI: 1.2–3.2). Compared to premolar teeth, caries experience was more likely to occur in maxillary molars (OR = 7.4: 95% CI: 6.6–8.3), mandibular molars (OR = 17.0, 95% CI: 15.3–18.2) and less likely to occur in incisors (OR = 0.55, 95% CI: 0.46–0.66). Compared to palatal/lingual surfaces caries experience was more likely (OR = 2.7, 95% CI 2.4–3.0) to occur at the buccal surface. The ICC estimate for individuals (level 3) amounted to 0.54 (95% CI 0.48–0.59), indicating that 54% and 46% of the variance in caries experience was attributable to variation between individuals and within individuals, respectively. The likelihood ratio test confirmed that ICC was different from zero and that a two-level model is justified and an appropriate approach to the present data ( $p = 0.0000$ ).

## Discussion

This study is among the first to report on caries experience in HIV-1 infected mothers as compared to HIV-1 negative controls living in a similar non-occidental socio-cultural setting. The prevalence of caries experience, untreated caries and gingival bleeding was high among both HIV-1 infected- and uninfected mothers amounting to 50% or above of the study population. Ordinary logistic regression with aggregated outcome measures of caries experience revealed significant odds for mothers who were HIV-1 infected, older aged, having higher education and gingival bleeding, whereas multilevel analyses of site specific

caries revealed significant odds for mother's age and gingival bleeding status. Socio-behavioral inequalities in dental caries experience were less marked, nor did socio-behavioral inequalities in dental caries differ between HIV-1 infected- and uninfected mothers. This supports evidence that the HIV-1 epidemic in low-income countries seem to be more generalized across the socio-economic spectrum, suggesting that HIV-1 positive and negative mothers are more socio-economically comparable [26]. We conclude that a multilevel random intercept model is appropriate and efficient for analyses of dental caries data in the context of HIV-1 infected Ugandan mothers. It improves the standard logistic regression approach by inclusion of covariates at site- and tooth level, A significant amount of variability was attributable to the between individual level implying that carious surfaces and teeth were more highly correlated within than between mothers. Although we aimed to fit a 3- level model with surfaces nested within teeth and teeth nested within individuals, there was hardly any variation of caries at tooth level.

Major strengths of this study are the use of novel statistical methods accounting for dependency in observations within individual as well as strict characterization of HIV-1 status and use of community controls [27]. Whereas models for dependent observations are well established in medical research, their application are limited in dentistry [28–30]. Previous studies applying a multilevel approach have been performed, most commonly, in the field of periodontology [31]. Yet, few studies are available utilizing multilevel analysis with hierarchical structured caries data [32]. A benefit of multilevel analysis is the possibility to separate variance estimates at different levels, allowing for estimation of intra class correlation at the individual and tooth level. This offers the advantage of more information of caries patterns within an individual. This study utilized both ordinary- and mixed effect logistic regression models, thus confirming inequalities in mothers' caries experience at individual and site specific levels. Estimates from ordinary logistic regression models with aggregate caries outcome measures define differences in caries experience among population groups having different characteristics. A mixed model logistic regression approach provides person specific estimates or change in odds for a specific mother according to her changes in characteristics. Despite difference in interpretation of the models and the estimates from the models, ordinary logistic- and mixed model logistic regression revealed comparable results. Some limitations should be considered, when interpreting our findings. The lack of statistically significant association of HIV-1 status with caries experience might be attributed to limited statistical power as mixed and random effect models are computationally intensive. Missing data and loss to follow-up among HIV-1 infected mothers might limit the interpretation of the findings as the present analyses might suffer from being underpowered. It is possible that caries prevalence in HIV-1 infected mothers is underestimated since only women passively followed up were included in the analyses and those who might have died before follow-up examination were not part of the group analyzed.

The prevalence of dental caries was high in this study population and matched previous estimates in the general Ugandan adult population amounting to 67% [33]. Mothers living with HIV-1 presented with a caries prevalence of 81%, being in accordance with previous estimates in comparable groups of Ugandan adults amounting to 83% [20]. HIV-1 infected mothers seemed to be at higher risk of developing dental caries compared to the uninfected controls. Although a specific measure of duration of HAART

medication was not available, in this study, HIV-1 infected mothers who were follow-up participants from the PROMISE PEP trial had been on systematic HAART medication for more than 6 years. Studies focusing caries among HIV-1 infected adults on HAART have not yet identified any specific trend [14, 20]. However, a recent Ugandan study reported on increased prevalence of dental caries according to longer duration of HAART medication [20]. Independent of mothers' HIV-1 status, findings from multilevel analysis indicated higher odds of caries in maxillary and mandibular molar teeth and lower odds in incisor teeth as compared to premolars. This supports well established evidence that caries varies according to different groups of teeth within individuals [34].

It is important to discuss the unexpected positive association between high education and caries experience as depicted in Table 3. This is contrary to previous findings among Ugandan adults living with HIV-1 showing an expected negative relationship between education level and dental caries [20]. In support of the present findings are studies from Africa showing higher prevalence of dental caries in people from less poor- compared to very poor households [35]. It is possible that the coding with only three categories have failed to capture the effect of education very well. It is also possible that this association reflects a higher F component among higher than lower educated since the highly educated are those most frequently using dental care services.

A positive association between gingival bleeding and dental caries accords with other findings reporting on higher probability of dental caries in people with poor than with good oral hygiene [32, 36]. While it appears that HAART reduces saliva flow with above 80% of the prescribed HAART medications causing xerostomia [14], HIV-1 infection might also decrease saliva irrespective of medication [14, 37]. Salivary gland hypofunction, xerostomia and HAART medication are among the most important risk factors of dental caries and periodontal disease in HIV-1 infected people.

## **Conclusions**

In summary, this study suggests that dental caries prevalence is higher in HIV-1 infected than in HIV-1 uninfected Ugandan mothers and varies with mothers, age, education and clinically recoded gingival inflammation. Socio-demographic differences in dental caries did not vary by HIV-1 status. We found that a multilevel random intercept model is appropriate and efficient for analyses of dental caries data in the context of HIV-1 infected and uninfected mothers. Based on the present findings we recommend that oral care- and preventive strategies are included into HIV-1 treatment programs.

## **Declarations**

## **Ethics approval and consent to participate**

Ethical clearance was obtained from the School of Medicine Research and Ethics committee, Makerere University (SOMREC)-REC – 030, Uganda National Council of Science and Technology (UNCST)-HS 2373

and the Regional Committee for Health and Medical Research (REK) – 2017/760/REC sør-øst C from Norway.

### **Consent for publication**

Not applicable

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare no competing interests

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## **Author contributions**

NB, AN, IMSE JKT, LTF and SAL made contributions to conception and design of the study. NB, AN and JKT contributed to data acquisition. NB, AN, IMSE, JKT, LTF and SAL analyzed, interpreted, drafted, and gave final approval to this version of the manuscript.

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## **Abbreviations**

AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral therapy

CI	Confidence interval
CIS	Child impact scale
CRF	Case record form
ECC	Early childhood caries
DMFT	Decayed missing filled teeth surfaces
DNA-PCR	Deoxyribonucleic acid Polymerase chain reaction
HAART	Highly active antiretroviral therapy
HIV	Human deficiency virus
HEU	HIV exposed uninfected
HUU	HIV unexposed uninfected
ICC	Inter class correlation
IQR	Interquartile range
LPV/r	Lopinavir/ritonavir
NVP	Niverapine
OR	Odds ratio
OLR	Ordinary logistic regression
PMTCT	Prevention of mother to child transmission
PROMISE-PEP	Promoting infant health and nutrition in Sub-Saharan Africa: Safety and efficacy of infant Peri-Exposure Prophylaxis
PROMISE-PEP-M&S	Promoting infant health and nutrition in Sub-Saharan Africa: Safety and efficacy of infant Peri-Exposure Prophylaxis to prevent HIV-1 transmission by breastfeeding-Mechanisms & Safety
RIM	Random intercept model
WHO	World Health Organization
WIHS	Womens interagency HIV Study

ZDV	Zidovudine
3TC	Lamivudine

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